REMARKS

I. Restriction Requirement

Applicants election of Group I claims is affirmed.

II. Claim Status

Claim 18 has been amended to incorporate the limitation of dependent claim 50. Claims 50, 54, 57, 59, and 73 have been canceled without prejudice to further prosecution in one or more related continuation or divisional applications. Claims 49, 51-53, 55-56, 58, 77-78, 81, and 189 have been amended. Claims 190-210, drawn to a non-elected invention, are cancelled without prejudice to further prosecution in one or more divisional or continuation applications. Claims 18, 20, 49, 51-53, 55-56, 58, 72, 74-81, 83, 131, 134, 181-189 are thus pending. The amendments do not introduce new matter into the Specification.

III. Specification

The Specification has been amended to capitalize trademark names and to remove embedded hyperlinks. Accordingly, Applicants respectfully request withdrawal of the objection to the specification on these grounds.

IV. Drawings

The Office Action indicates that corrected drawings are required because the drawings allegedly contain too many nucleic and amino acid sequences which are not identified specifically by sequence identification number. Applicants respectfully wish to point out that all of the sequences in the drawings are identified by a sequence identification number. Corrected drawings, however, are being provided to remove the sequence names from the drawings in order to make the sequence identification numbers more readily visible.

V. Rejections

A. 35 U.S.C. § 112, First Paragraph – Written Description

Claims 18, 72-81, 83 131, 134 and 181 stand rejected under 35 U.S.C. § 112, first paragraph, for containing subject matter which allegedly was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed. This rejection is respectfully traversed in view of the pending claims.

The Office Action asserts that the claims at issue do not satisfy the written description requirement because the specification allegedly does not describe structure/activity "in the single disclosed species." (Office Action at page 7, paragraph 5) It is also alleged that only six species are disclosed that fall under the claims.

Claim 18, as amended, is directed to an isolated or recombinant polypeptide having lipase activity and comprising a sequence having at least 94% amino acid sequence identity to the mature region of SEQ ID NO: 55. Contrary to the assertion in the Office Action, the specification actually discloses 34 species that fall under the claimed genus. All of the following species having a sequence identity of at least 94% to the mature region of SEQ ID NO: 55: SEQ ID NOS. 58 (98%), 59 (98%), 60 (96%), 61 (98%), 62 (98%), 75 (96%), 76 (96%), 77 (96%), 78 (97%), 80 (96%), 81 (96%), 82 (96%), 83 (96%), 84 (96%), 85 (95%), 86 (95%), 87 (96%), 88 (95%), 89 (94%), 94 (96%), 95 (95%), 96 (96%), 97 (97%), 98 (97%), 99 (97%), 100 (97%), 101 (96%), 102 (96%), 103 (97%), 104 (98%), 105 (97%), 106 (96%), 107 (97%), and 108 (98%).

There is actual reduction to practice of these 34 representative species of the genus claimed in claim 18, and the sequences of these species are depicted in the table on pages 113-141, Figure 5-6, and in the Sequence Listing of the application.

Of the 34 species described, 33 species have a sequence identity that is at least 95% identical to the mature region of SEQ ID NO: 55; 29 species have a sequence identity that is at least 96% identical to the mature region of SEQ ID NO: 55; 14 species have a sequence identity that is at least 97% identical to the mature region of SEQ ID NO: 55; and 6 species have a sequence identity that is at least 98% identical to the mature region of SEQ ID NO: 55.

Applicants claims are of the type described in Example 14 of the Written Description Guidelines[1]. As in that Example, Applicants claim a polypeptide having a percent identity to a reference sequence and possessing an enzymatic activity. Similar to that Example, procedures for making such polypeptides are conventional in the art, and are even further described in the Specification (for example, at page 45, line 16 to page 47, line 7 and at page 59, line 1 to page 73, line 29). Likewise, an assay is described for identifying other polypeptides having the claimed lipase activity, for example, at page 45, line 16 to page 47, line 7 and at page 21, lines 25-28, and Example 1.

In contrast to Example 14 of the Written Description Guidelines which discloses only one species of the claimed genus, Applicants have described 34 species. The analysis in the Written Description Guidelines concluded that the single species disclosed in Example 14 of the Guidelines was representative of the claimed genus and that the disclosure met the written description requirement of 35 U.S.C. § 112. With respect to the claimed invention, Applicants respectfully submit that the claimed genus does not embrace substantial variation among the sequences being claimed. Moreover, in the Specification, the Applicants provide the sequences of a large number of species that fall under the claimed genus to demonstrate that they had full possession of the claimed invention at the time the application was filed. In view of this, the Specification meets the requirements of 35 U.S.C. § 112, as clarified by case law and the U.S.P.T.O. Written Description Guidelines. Withdrawal of the written description rejection is therefore respectfully requested.

B. 35 U.S.C. § 112, First Paragraph – Enablement

Claims 18, 50-59, 72-81, 83, 131, 134, and 181-189 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly being non-enabling with respect to the scope of the claims. This rejection is respectfully traversed in view of the pending claims.

The Office Action alleges that the amount of experimentation required to identify naturally or man-made polypeptides having 94-98% sequence identity to SEQ ID NO: 55, and having a

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[1] Example 14 of the Written Description Guidelines:
Claim: A protein having SEQ ID NO: 3 and variants thereof that are at least 95% identical to SEQ ID NO: 3 and catalyze the reaction of A → B.

particular chemical or biological function such as enantioselective lipase activity is enormous. It is further alleged that information regarding the biological source of the polypeptide, the utility of the variant polypeptide and its chemical properties, the amino acid that can be deleted inserted or substituted without adverse effect on a desired function must be provided, otherwise the amount of experimentation is undue. Applicants respectfully disagree.

The enablement requirement has been construed to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 8 USPQ2d at 1404 (Fed. Cir. 1988); see also *United States v. Telectronics, Inc.*, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988) ("The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation.") The factors to be considered include (1) the quantity of experimentation necessary; (2) the amount of direction or guidance presented; (3) the presence or absence of working examples; (4) the nature of the invention; (5) the state of the prior art; (6) the relative skill of those in the art; (7) the predictability or unpredictability of the art; and (8) the breadth of the claims. *Id.* It is not proper to conclude that a disclosure is not enabling based on an analysis of only one of the above factors while ignoring one or more of the others. MPEP at § 21604.01(a).

Independent claim has been amended to specify that the claimed polypeptides have lipase activity. Thus, with respect to factor (8), the claims require that the polypeptide have a minimum of 94% identity to SEQ ID NO: 55, and have lipase activity.

With respect to factors (1), (2), and (3), the disclosure provides ample guidance as to how to make the claimed polypeptides using mutagenesis and recombination methods (Specification at page 59, line 1 to page 73, line 29) and how to screen those polypeptides using the assays described in Examples I and II, as well as how to screen in high throughput format, which is described at page 74, line 1 to page 75, line 2. The Specification describes how to screen for lipase activity using soybean oil as substrate (Example I) and how to screen for enantioselectivity using neryl butyrate or geranyl butyrate as substrate (Example II and at page 24, line 3 to page 26, line 7). A description of how to identify natural lipases and recombine them to create homologues is described at page 22, line 26 to page 23, line 25. A description of how to screen for enantioselectivity is provided, *inter alia*, at page 24, line 3 to page 25, line 9, and Example II. A description of what sequence substitutions to make

is provided at page 26, lines 9-21. A description of preferred substitutions observed to correspond to enantioselectivity for gernyl butyrate vs. neryl butyrate is provided at page 26, lines 22-29. A description of preferred substitutions observed to correspond to enantioselectivity for neryl butyrate vs. geranyl butyrate is provided at page 26, line 30 to page 27, line 6. The Specification further describes making conservative substitutions to generate variants at page 45, line 15 to page 47, line 7. A description of how to generate additional lipase variants is further provided at page 27, line 7-9 (via recombination of polynucleotides corresponding to SEQ ID NO: 1 through SEQ ID NO: 54).

With respect to factors (4) and (5), the invention is directed to polypeptides having lipase activity and a sequence that does not substantially vary from SEQ ID NO: 55. The disclosure includes citations to many publications that report the use of mutagenesis and recombination methods to generate variants.

With respect to factor (6), the use of the aforementioned recombination and mutagenesis methods are well known to those having ordinary skill in the art. It is respectfully submitted that a skilled person in the art would not consider the quantity of experimentation necessary to practice the claimed invention undue in view of what was known in the prior art and the ample guidance provided in Applicants' disclosure.

With respect to factor (7), "'predictability or lack therof' in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention." MPEP at § 2164.03. Applicants have provided a large number of polypeptides that meet the requirements of the claims, methods for generating variants and methods for screening the variants. It is well within the ability of a skilled person in the art to either practice the described methods in order to generate additional variants or to make the numerous variants specifically described in the application that are within the scope of the claims.

The enablement requirement of the first paragraph of § 112 requires no more than a disclosure sufficient to enable one of skill in the art to practice the full scope of the claimed invention without undue experimentation. It is respectfully submitted that, in view of the teaching provided in Applicants' disclosure, the state of the prior art at the time of the filing of the present application, and the skill level of the practitioner in the art, that the disclosure is enabling as to the full scope of the pending claims. In view of the discussion above, Applicants respectfully submit

that the disclosure satisfies the requirements of the enablement requirement under 35 U.S.C. § 112, first paragraph. Accordingly, withdrawal of this rejection is respectfully requested.

C. 35 U.S.C. § 112, Second Paragraph

Claims 53-55, 57-59, 73, 77, 78, 81, and 189 stand rejected under 35 U.S.C. § 112, second paragraph, as being allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as their invention. This rejection is respectfully traversed in view of the pending claims.

The rejections to claims 54, 57, 59, and 73 are rendered moot by the cancellation of these claims.

Claim 53 has been rejected for having an undefined abbreviation for DMF. Claim 53 has been amended to refer to the well known definition of DMF, i.e., N,N-dimethylformamide. Claim 78 has been rejected for containing undefined abbreviations of FLAG and GST, and for referring to a "GST fusion." Claim 78 has been amended to refer to the well known definition of GST, i.e., glutathione S-transferase, and to delete the term "fusion" and the trademark, FLAG.

Claim 55 has been rejected because the term "neryl-butyrate" is allegedly indefinite. Applicants respectfully submit that "neryl-butyrate" is a well known compound and is sold under that name by Sigma-Aldrich (St. Louise, MO). The Sigma-Aldrich catalog provides the structure as $C_{14}H_{24}O_2$. The relevant pages of the catalog (from the Sigma-Aldrich online catalog) are attached.

Claim 77 has been rejected because the term "polypeptide purification subsequence" is allegedly indefinite. This claim has been amended to refer to "polypeptide purification domain." Support for this amendment can be found in the Specification at page 87, lines 1-7.

Claim 81 has been rejected because the term "an organic derivatizing agent" is allegedly indefinite. To expedite prosecution, claim 81 has been amended to delete reference to this term.

Claim 189 has been rejected because the term "under stringent conditions" is allegedly indefinite. This claim has been amended to incorporate the conditions referred to in the Specification at page 49, lines 1-5.

In view of the above amendments, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 112, second paragraph.

D. 35 U.S.C. § 102

Claim 189 stands rejected under 35 U.S.C. § 102(b) as being allegedly anticipated by Dartois et al. This rejection is respectfully traversed in view of the pending claims.

The Office Action alleges that Dartois et al. teach a nucleic acid that would hybridize to SEQ ID NO: 1 and that the polypeptide of Dartois et al. contains more than 45 contiguous amino acid residues identical to SEQ ID NO: 55, including certain residue/position combinations that are specified in claim 189. Applicants respectfully wish to clarify that the claim requires that the encoded polypeptide have one or more specific residues at positions that are equivalent amino acid positions relative to SEQ ID NO: 75 (see explanation in the Specification at page 22, lines 6-17 and at page 26, lines 9-21). SEQ ID NO: 75 encodes the mature region of a lipase, whereas the polypeptide in Figure 2 of the Dartois et al. reference appears to include the signal peptide as well as the mature region.

Using the CLUSTALW alignment program, position 1 of SEQ ID NO: 75 aligns with position 33 of the polypeptide in Figure 2 of the Dartois et al. reference (see Dartois et al. Figure 2, line 10, beginning at "EHNPVVMVH . . ." and compare to SEQ ID NO: 75, "EHNPVVMVH . . ."—position 1 corresponds to "E", position 2 corresponds to "H", and so on).

After aligning the Dartois et al. polypeptide sequence in Figure 2 with SEQ ID NO: 75, the following residues in the Dartois et al. sequence occupy the equivalent amino acid positions specified in claim 189 (the claimed residue is also provided for comparison):

Equivalent Position	Residue in Dartois et al.	Claimed Residue
1	Glu/E	Lys/K
14	Ala/A	Thr/T
17	Asn/N	Ser/S
22	Lys/K	Arg/R
26	Val/V	Glu/E
31	Ser/S	Pro/P
33	Asp/D	Gly/G
34	Lys/K	Glu/E
35	Leu/L	Pro/P

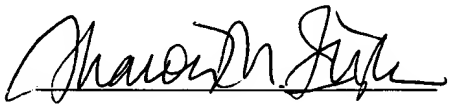
37	Ala/A	Pro or Thr/P or T
41	Trp/W	Ser or Lys/S or K
42	Asp/D	Gly/G
43	Lys/K	Arg or Glu/R or E
61	Val/V	Ala/A
75	His/H	Tyr/Y
96	Ala/A	Gly/G
97	Asn/N	Ser/S
104	Ala/A	Thr/T
107	Leu/L	Ser/S
125	Thr/T	Ala/A
129	Ser/S	Gly/G
134	Ile/I	Val/V
138	Tyr/Y	Cys/C
141	Arg/R	Lys/K
146	Arg/R	Lys/K
156	Ile/I	Thr/T
160	Tyr/Y	Met/M
166	Ser/S	Arg/R
177	Gln/Q	His/H

Claim 189 requires that the claimed polypeptide have one or more specific amino residues in equivalent positions determined by alignment to SEQ ID NO: 75. Claim 189 has been amended to recite that the "polypeptide is encoded by a polynucleotide that hybridizes under stringent conditions. . . ." The polypeptide depicted in Figure 2 of the Dartois et al. reference has none of the residues specified and therefore, does not anticipate claim 189. Accordingly, withdrawal of the rejection under 35 U.S.C. § 102(b) is respectfully requested.

CONCLUSION

In view of the amendments and remarks provided above, it is respectfully submitted that the pending claims are in condition for allowance and notification to that effect is respectfully requested. Should the Examiner believe that a telephone conference would expedite the prosecution of this application, the undersigned can be reached at the telephone number set forth below. The Commissioner is hereby authorized to charge any deficiency in fees or credit any overpayment to Deposit Account No. 50-0990.

April 1, 2004

By: 

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Related Documents

MSDS

Lot Specific Information

Certificate of Analysis

Lot #:

Specification Sheet

Options

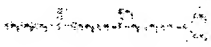
Print Preview
Bulk Quote
Ask A Scientist

Product No.	Description
W277401	**Neryl butyrate** 90+ %

Register or Login for pricing and availability

Identifiers

Molecular Formula	$C_{14}H_{24}O_2$
Molecular Weight	224.34
CAS Number	999-40-6
FEMA Number	2774
Council of Europe no.	505



Zoom In

Description

Features and Benefits	Sweet, leafy, floral, delicate, orange

Properties

bp	240 °C/760 mm Hg (lit.)

References

Beilstein reference	*Beil.* **2**,248 *Arctander*, 2324 *FT-IR* **2**(1), 1018:B *Fenaroli*, 592